WHAT IS CLAIMED:

1. A method for detecting a polymorphism in a polynucleotide, comprising:

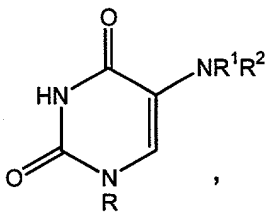
providing a target polynucleotide;

replacing a natural nucleotide at greater than 90% of its points of occurrence in the target polynucleotide, provided the points of occurrence are not in a primer sequence, by amplification or primer extension using a base-modified nucleotide and three natural nucleotides to give a modified target polynucleotide;

contacting the modified target polynucleotide with a reagent or combination of reagents that cleaves it at greater than 90% of the base-modified nucleotides to give a set of fragments; and,

analyzing the fragments to detect a polymorphism,

wherein the base-modified nucleotide comprises the following structure:



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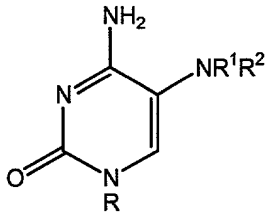

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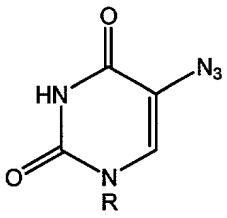

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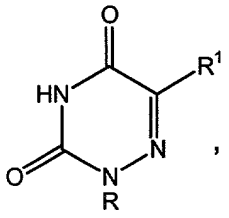

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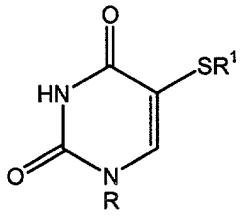

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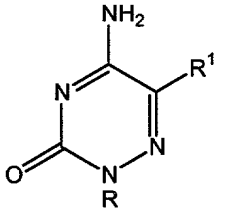

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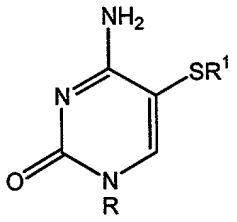
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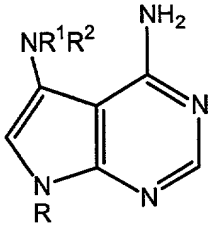
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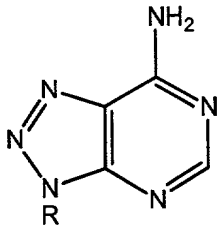
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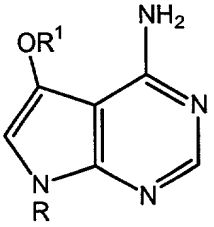
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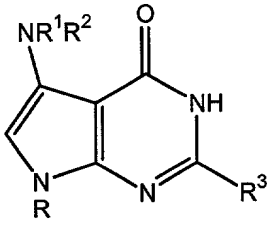
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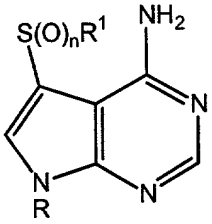
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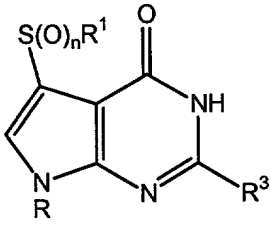
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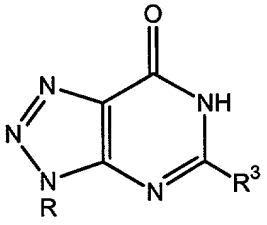
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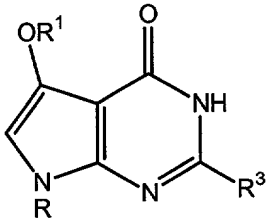
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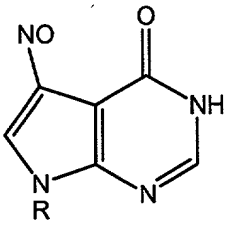
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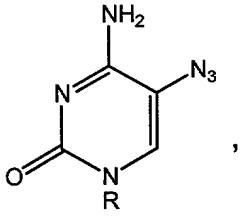
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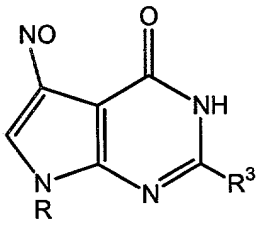
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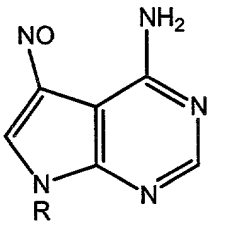
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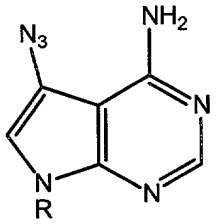
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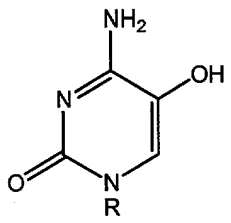

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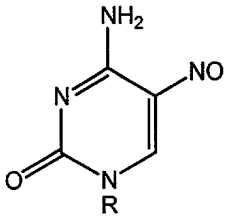

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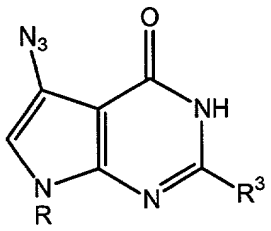

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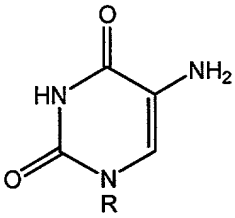

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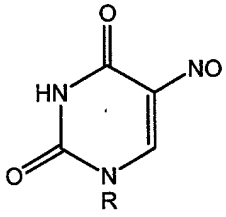

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wherein:

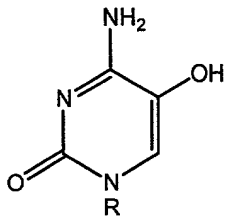
R is a ribose or a deoxyribose moiety of a polynucleotide;

R^1 and R^2 are independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkenyl, alkynyl, aryl, aralkyl and alkaryl, wherein, if R^1 or R^2 contains two or more contiguous methylene (- CH_2-) groups, any two such methylene groups may have interjected between them a group selected from the group consisting of -O-, -C(O)NH-, -C(O)NHC(O)-, -NH-, -C(S)NH-, -CO-, -CS-, -S- and $(-CF_2-)_m$, wherein m is 1- 10;

R^3 is hydrogen or $-NH_2$; and,

n is 0, 1 or 2.

2. The method of claim 1, wherein the base-modified nucleotide has the chemical structure:



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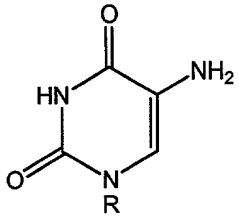

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wherein R is a ribose or deoxyribose moiety of an oligonucleotide.

3. The method of claim 2, wherein contacting the modified polynucleotide with a reagent or reagents comprises contacting it with a chemical base.

4. The method of claim 3, wherein the chemical base comprises a secondary amine having a boiling point above 100° C at atmospheric pressure.

5. The method of claim 4, wherein the secondary amine has a boiling point above 150° C at atmospheric pressure.

6. The method of claim 4, wherein the secondary amine has a boiling point above 200° C at atmospheric pressure.

7. The method of claim 6, wherein the secondary amine is selected from the group consisting of 3-pyrrolidinol, 2-pyrrolidinemethanol, 3-pyrrolidinemethanol, 4-hydroxypiperidine and 4-piperidineethanol.

8. The method of claim 1, wherein analysis of the fragments comprises gel electrophoresis.

9. The method of claim 1, wherein analysis of the fragments comprises mass spectrometry.

10. The method of claim 9, wherein mass spectrometry comprise MALDI mass spectrometry.

11. The method of claim 9, wherein in mass spectrometry comprises ESI mass spectrometry.

12. The method of claim 9, wherein analyzing the fragments comprises comparing the masses of the fragments with masses of fragments predicted if the polymorphism is present or with masses of fragments predicted if the polymorphism is not present.

13. A method for detecting a polymorphism in a polynucleotide, comprising:

replacing a natural nucleotide at greater than 90% of its points of occurrence in the target polynucleotide, provided the points of occurrence are not in a primer sequence, with a modified nucleotide to give a modified target polynucleotide;

contacting the modified target polynucleotide with a secondary amine having a boiling point greater than 100° C at atmospheric pressure, at a temperature that results in cleavage of the modified target polynucleotide at greater than 90% of the modified nucleotides to give a set of fragments; and,

analyzing the fragments to detect a polymorphism.

14. The method of claim 13, wherein the secondary amine has a boiling point greater than 150° C at atmospheric pressure.

15. The method of claim 13, wherein the secondary amine has a boiling point greater than 200° C at atmospheric pressure.

16. The method of claim 15, wherein the secondary amine is selected from the group consisting of 3-pyrrolidinol, 2-pyrrolidinemethanol, 3-pyrrolidinemethanol, 4-hydroxypiperidine and 4-piperidineethanol.

17. The method of claim 1 or claim 13, wherein the polynucleotide is contacted with a chemical oxidant prior to contact with the secondary amine.

18. The method of claim 17, wherein the chemical oxidant comprises potassium permanganate.

19. The method of claim 1 or claim 13, wherein the percentage replacement of a natural nucleotide with a modified nucleotide, the percentage cleavage of a modified polynucleotide or both the percentage replacement and the percentage cleavage is greater than 95%.

20. The method of claim 1 or claim 13, wherein the percentage replacement of a natural nucleotide with a modified nucleotide, the percentage cleavage of a modified polynucleotide or both the percentage replacement and the percentage cleavage is greater than 99%.